



TECH CENTER 1600/2900

JUL 03 2002

RECEIVED

Under Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Approved for use through 10/31/2002. OMB 0851-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A/PTO			<b>Complete if Known</b>		
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			Application Number	10/025,170	
			Filing Date	December 18, 2001	
			First Named Inventor	Antonio Iavarone	
			Art Unit	TBA	
			Examiner Name	TBA	
Sheet	1	of	6	Attorney Docket Number	96700/709

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				

Examiner Signature	Date Considered
-----------------------	--------------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid control number.

PTO/SB/08B (10-99)  
Approved for use through 10/31/2002. OMB 0651-0094  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

RECEIVED  
JUL 03 2002

Substitute for form 1449B/PTO		<b>Complete if Known</b>			
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/025,170		
		Filing Date	December 18, 2001		
		First Named Inventor	Antonio Iavarone		
		Group Art Unit	TBA		
		Examiner Name	TBA		
Sheet	2	of	6	Attorney Docket Number	96700/709

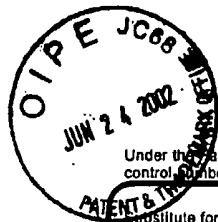
OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
SU	1	ALEVIZOPOULOS et al., Cyclin E and c-Myc promote cell proliferation in the presence of p16INK4a and of hypophosphorylated retinoblastoma family proteins. EMBO J., 16:5322-33, 1997.	
	2	BIGGS et al., A human Id-like helix-loop-helix protein expressed during early development. Proc. Natl. Acad. Sci. USA, 89:1512-16, 1992.	
	3	BORDOW et al., Prognostic significance of MYCN oncogene expression in childhood neuroblastoma. J. Clin. Oncol., 16:3286-94, 1998.	
	4	BOYD et al., c-Myc target gene specificity is determined by a post-DNA-binding mechanism. Proc. Natl. Acad. Sci. USA, 95:13887-92, 1998.	
	5	BRODEUR et al., Neuroblastoma. Effect of genetic factors on prognosis and treatment. Cancer, 70:1685-94, 1992.	
	6	CANCE et al., Altered expression of the retinoblastoma gene product in human sarcomas. N. Engl. J. Med., 323:1457-62, 1990.	
	7	CHAN et al., MYCN protein expression as a predictor of neuroblastoma prognosis. Clin. Cancer Res., 3:1699-706, 1997.	
	8	CLARKE et al., Requirement for a functional Rb-1 gene in murine development. Nature, 359:328-30, 1992.	
	9	COHN et al., MYCN expression is not prognostic of adverse outcome in advanced-stage neuroblastoma with nonamplified MYCN. J. Clin. Oncol., 18:3604-13, 2000.	
	10	COOPER et al., Expression of the Id family helix-loop-helix regulators during growth and development in the hematopoietic system. Blood, 89:3155-65, 1997.	
	11	CORDON-CARDO et al., Altered expression of the retinoblastoma gene product: prognostic indicator in bladder cancer. J. Natl. Cancer Inst., 84:1251-56, 1992.	

Examiner Signature		Date Considered	10/4/04
--------------------	--	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burdan Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 3 of 6

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

### Complete if Known

Application Number	10/025,170
Filing Date	December 18, 2001
First Named Inventor	Antonio Iavarone
Group Art Unit	TBA
Examiner Name	TBA
Attorney Docket Number	96700/709

TECH CENTER 16002900

JUL 03 2002

RECEIVED

### OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cita No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
See	12	DYSON, N., The regulation of E2F by pRB-family proteins. Genes & Dev., 12:2245-62, 1998.	
	13	FLORIO et al., Id2 promotes apoptosis by a novel mechanism independent of dimerization to basic helix-loop-helix factors. Mol. Cell. Biol., 18:5435-44, 1998.	
	14	GOODRICH and LEE, Abrogation by c-Myc of G1 phase arrest induced by RB protein but not by p53. Nature, 360:177-179, 1992.	
	15	HIRNING et al., A comparative analysis of N-myc and c-myc expression and cellular proliferation in mouse organogenesis. Mech. Dev., 33:119-25, 1991.	
	16	HIYAMA et al., Immunohistochemical analysis of N-myc protein expression in neuroblastoma: correlation with prognosis of patients. J. Pediatr. Surg., 26:838-43, 1991.	
	17	IAVARONE et al., The helix-loop-helix protein Id-2 enhances cell proliferation and binds to the retinoblastoma protein. Genes & Dev., 8:1270-84, 1994.	
	18	IAVARONE and MASSAGUE, E2F and histone deacetylase mediate transforming growth factor beta repression of cdc25A during keratinocyte cell cycle arrest. Mol. Cell. Biol., 19:916-22, 1999.	
	19	ISHIGURO et al., Expression of Id2 and Id3 mRNA in human lymphocytes. Leuk. Res., 19:989-96, 1995.	
	20	ISHIGURO et al., Id2 expression increases with differentiation of human myeloid cells. Blood, 87:5225-31, 1996.	
	21	JACKS et al., Effects of an Rb mutation in the mouse. Nature, 359:295-300, 1992.	
	22	JEN et al., Expression patterns of Id1, Id2, and Id3 are highly related but distinct from that of Id4 during mouse embryogenesis. Dev. Dyn., 207:235-52, 1996.	

Examiner Signature	<i>Lusen</i>	Date Considered	10/4/04
--------------------	--------------	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Approved for use through 10/31/2002. OMB 0851-0073  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

RECEIVED  
JUL 03 2002

Substitute for form 1449B/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		<b>Application Number</b>	10/025,170
(use as many sheets as necessary)		<b>Filing Date</b>	December 18, 2001
		<b>First Named Inventor</b>	Antonio Iavarone
		<b>Group Art Unit</b>	TBA
		<b>Examiner Name</b>	TBA
		<b>Attorney Docket Number</b>	96700/709
Sheet	4	of	6

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials <sup>2</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
Su	23	JEN et al., Each member of the Id gene family exhibits a unique expression pattern in mouse gastrulation and neurogenesis. Dev. Dyn., 208:92-106, 1997.	
	24	KLEEF et al., The helix-loop-helix protein Id2 is overexpressed in human pancreatic cancer. Cancer Res., 58:3769-72, 1998.	
	25	KRATZKE et al., Rb and p16INK4a expression in resected non-small cell lung tumors. Cancer Res., 56:3415-20, 1996.	
	26	LASORELLA et al., Id2 specifically alters regulation of the cell cycle by tumor suppressor proteins. Mol. Cell. Biol., 16:2570-78, 1996.	
	27	LASORELLA et al., Id2 is a retinoblastoma protein target and mediates signalling by Myc oncoproteins. Nature, 407:592-98, 2000.	
	28	LEE et al., Mice deficient for Rb are nonviable and show defects in neurogenesis and haematopoiesis. Nature, 359:288-94, 1992.	
	29	LEE et al., Dual roles of the retinoblastoma protein in cell cycle regulation and neuron differentiation. Genes & Dev., 8:2008-21, 1994.	
	30	LYDEN et al., Id1 and Id3 are required for neurogenesis, angiogenesis and vascularization of tumour xenografts. Nature, 401:670-77, 1999.	
	31	MARIS and MATTHAY, Molecular biology of neuroblastoma. J. Clin. Oncol., 17:2264-79, 1999.	
	32	MARTINSEN and BRONNER-FRASER, Neural crest specification regulated by the helix-loop-helix repressor Id2. Science, 281:988-91, 1998.	
	33	MASSARI and MURRE, Helix-loop-helix proteins: regulators of transcription in eucaryotic organisms. Mol. Cell. Biol., 20:429-40, 2000.	

Examiner Signature	Date Considered
<i>[Signature]</i>	10/4/04

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Under the Patent Work Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

PTO/SB/08B (10-91)  
Approved for use through 10/31/2002. OMB 0651-0001  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

RECEIVED  
JUL 03 2002

Substitute for form 1449B/PTO		<b>Complete if Known</b>			
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>		Application Number	10/025,170		
		Filing Date	December 18, 2001		
		First Named Inventor	Antonio Iavarone		
		Group Art Unit	TBA		
		Examiner Name	TBA		
Sheet	5	of	6	Attorney Docket Number	96700/709

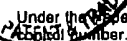
OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
SM	34	MORI et al., Lactation defect in mice lacking the helix-loop-helix inhibitor Id2. EMBO Journal, 19:5772-5781, 2000.	
	35	MORROW et al., Overexpression of the Helix-Loop- Helix protein Id2 blocks T cell development at multiple stages. Mol. Immunol., 36:491-503, 1999.	
	36	MULLIGAN and JACKS, The retinoblastoma gene family: cousins with overlapping interests. Trends Genet., 14:223-29, 1998.	
	37	NEUMAN et al., Neuronal expression of regulatory helix-loop-helix factor Id2 gene in mouse. Dev. Biol., 160:186-195, 1993.	
	38	NEUMAN et al., Helix-loop-helix transcription factors regulate Id2 gene promoter activity. FEBS Lett., 374:279-83, 1995.	
	39	NORTON et al., Id helix-loop-helix proteins in cell growth and differentiation. Trends Cell Biol., 8:58-65, 1998.	
	40	NORTON, ID helix-loop-helix proteins in cell growth, differentiation and tumorigenesis. J. Cell Sci., 113:3897-905, 2000.	
	41	PIETENPOL et al., TGF-beta1 Inhibition of c-Myc transcription and growth in keratinocytes is abrogated by viral transforming protein with pRB binding domains. Cell, 61:777-85, 1990.	
	42	SELLERS and KAELEN, Role of the retinoblastoma protein in the pathogenesis of human cancer. J. Clin. Oncol., 15:3301-12, 1997.	
	43	SLACK et al., A critical temporal requirement for the retinoblastoma protein family during neuronal determination. J. Cell Biol., 140:1497-1509, 1998.	
	44	TOMA et al., Evidence that helix-loop-helix proteins collaborate with retinoblastoma tumor suppressor protein to regulate cortical neurogenesis. J. Neurosci., 20:7648-56, 2000.	

Examiner Signature	<i>[Signature]</i>	Date Considered	10/4/02
--------------------	--------------------	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE  
I intend to respond to a collection of information unless it contains a valid OMB

**TECH COMPUTER 1600/2900**

*(use as many sheets as necessary)*

Sheet 6 of 6

<b>Application Number</b>	10/025,170
<b>Filing Date</b>	December 18, 2001
<b>First Named Inventor</b>	Antonio Iavarone
<b>Group Art Unit</b>	TBA
<b>Examiner Name</b>	TBA
<b>Attorney Docket Number</b>	96700/709

[illegible]

**Date**  
**Considered**

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:** Assistant Commissioner for Patents, Washington, DC 20231.